

32 9. (Amended) A recombinant adeno-associated virus (rAAV) vector comprising a heterologous nucleotide sequence encoding B-domain deleted factor VIII operably linked with a liver-preferred enhancer and an AAV ITR wherein the only promoter driving expression of said B-domain deleted factor VIII is the AAV ITR.

33 12. (Amended) The rAAV vector of claim 9, wherein said liver-preferred expression control element comprises the hepatitis B virus EnhI enhancer given as about nucleotides 150-278 of the nucleotide sequence set forth in SEQ ID NO:1.

34 18. (Twice amended) A recombinant adeno-associated virus (rAAV) vector comprising a heterologous nucleotide sequence encoding a B-domain deleted factor VIII operably linked with an enhancer and an AAV ITR wherein the only promoter driving expression of said B-domain deleted factor VIII is the AAV ITR and wherein said heterologous nucleotide sequence is selected from the group consisting of:

- (a) the nucleotide sequence given as nucleotides 419 to 4835 of the nucleotide sequence set forth in SEQ ID NO:1,
- (b) a nucleotide sequence that hybridizes to the nucleotide sequence of (a) under conditions of high stringency and which encodes a biologically active B-domain deleted factor VIII, wherein the conditions of high stringency comprise hybridization in 25% formamide and 5X SSC at 42°C and at least one wash in 0.3 M NaCl, 0.03 M sodium citrate at 60°C; and
- (c) a nucleotide sequence that differs from the nucleotide sequences of (a) and (b) above due to the degeneracy of the genetic code, and which encodes a biologically active B-domain deleted factor VIII.

35 58. (Amended) A nucleic acid molecule comprising a nucleotide sequence encoding B-domain deleted factor VIII operably linked with a hepatitis virus enhancer and an AAV ITR

wherein the only promoter driving expression of said B-domain deleted factor VIII is the AAV ITR.

59. (Amended) The nucleic acid molecule of claim 58, wherein said hepatitis virus enhancer is from a hepatitis B virus.

60. (Amended) The nucleic acid molecule of claim 59, wherein said hepatitis virus enhancer is a hepatitis B virus EnhI or EnhII enhancer.

61. (Amended) The nucleic acid molecule of claim 60, wherein said hepatitis virus enhancer is a hepatitis B virus EnhI enhancer.

62. (Amended) The nucleic acid molecule of claim 58, wherein said nucleic acid molecule comprises the sequence given as about nucleotides 150 to 4835 of the nucleotide sequence set forth in SEQ ID NO:1.

63. (Amended) The nucleic acid molecule of claim 62, wherein said nucleic acid molecule further comprises a polyadenylation sequence.

64. (Amended) The nucleic acid molecule of claim 63, wherein said nucleic acid molecule comprises the sequence given as nucleotides 150 to 4914 of the nucleotide sequence set forth in SEQ ID NO:1.

65. (Amended) A vector comprising the nucleic acid molecule of claim 58.

68. (Amended) A recombinant adeno-associated virus (rAAV) vector comprising a heterologous nucleotide sequence operably linked with an enhancer and an AAV ITR wherein the only promoter driving expression of said B-domain deleted factor VIII is the AAV ITR and

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wherein said heterologous nucleotide sequence is at least 75% identical to nucleotides 419-4835 of SEQ ID NO:1 and encodes a biologically active B-domain deleted factor VIII.

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73. (Amended) A recombinant adeno-associated virus (rAAV) vector comprising a heterologous nucleotide sequence operably linked with a hepatitis virus enhancer and an AAV ITR wherein the only promoter driving expression of said B-domain deleted factor VIII is the AAV ITR and [expression control element,] wherein said heterologous nucleotide sequence is at least 75% identical to nucleotides 419-4835 of SEQ ID NO:1 and encodes a biologically active B-domain deleted factor VIII.

74. (Amended) The rAAV vector of claim 73, wherein said hepatitis virus enhancer is from hepatitis B virus.

75. (Amended) The rAAV vector of claim 74, wherein said hepatitis virus enhancer is a hepatitis B virus EnhI or EnhII enhancer.

76. (Amended) The rAAV vector of claim 75, wherein said rAAV vector comprises the sequence given as about nucleotides 150 to 4835 of the nucleotide sequence set forth in SEQ ID NO:1.

77. (Amended) The rAAV vector of claim 73, wherein said rAAV vector further comprises a polyadenylation sequence.

79. (Amended) A cell comprising the rAAV vector of claim 77.

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80. (Amended) A recombinant adeno-associated virus (rAAV) vector comprising a heterologous nucleotide sequence operably linked with an enhancer and an AAV ITR wherein the only promoter driving expression of said B-domain deleted factor VIII is the AAV ITR and

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wherein said heterologous nucleotide sequence encodes the amino acid sequence set forth in
SEQ ID NO:2.

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82. (Amended) A recombinant adeno-associated virus (rAAV) vector comprising a heterologous nucleotide sequence operably linked with at least one enhancer and an AAV ITR wherein the only promoter driving expression of said B-domain deleted factor VIII is the AAV ITR and wherein said heterologous nucleotide sequence is at least 75% identical to nucleotides 419-4835 of SEQ ID NO:1 and encodes a biologically active B-domain deleted factor VIII.

Please add new claims 91 and 92:

91. (New) The method of claim 1, wherein said rAAV vector is capable of expressing B-domain deleted factor VIII at a level sufficient for treatment of a factor VIII associated-disorder.

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92. (New) A recombinant adeno-associated virus (rAAV) vector comprising a heterologous nucleotide sequence encoding B-domain deleted factor VIII operably linked with at least one enhancer and an AAV ITR, wherein the only promoter driving expression of said B-domain deleted factor VIII is the AAV and said rAAV vector is capable of expressing B-domain deleted factor VIII at a level sufficient for treatment of a factor VIII associated-disorder.